adenosine deaminase 2 deficiency

Adenosine deaminase 2 (ADA2) deficiency is a disorder characterized by abnormal inflammation of various tissues, particularly the blood vessels (vasculitis). Signs and symptoms can begin anytime from early childhood to adulthood. The severity of the disorder also varies, even among affected individuals in the same family.

Inflammation is a normal immune system response to injury and foreign invaders (such as bacteria). However, the uncontrolled inflammation that occurs in ADA2 deficiency can damage many of the body's tissues and organs, including the skin, gastrointestinal system, kidneys, and nervous system. Depending on the severity and location of the inflammation, the disorder can cause disability or be life-threatening. Features that have been described in people with ADA2 deficiency include fevers that are intermittent, meaning they come and go; areas of net-like, mottled skin discoloration called livedo racemosa; an enlarged liver and spleen (hepatosplenomegaly); and recurrent strokes affecting structures deep in the brain that can start in the first few years of life. ADA2 deficiency causes mild immune system abnormalities in some individuals, but it is usually not associated with a significantly increased risk of bacterial and viral infections.

ADA2 deficiency is sometimes described as a form of polyarteritis nodosa (PAN), a disorder that causes inflammation of blood vessels throughout the body (systemic vasculitis). However, not all researchers classify ADA2 deficiency as a type of PAN.

Frequency

Only a few dozen individuals with ADA2 deficiency have been described in the medical literature. However, researchers suspect that it may not be a rare disease. They are working to determine whether ADA2 deficiency could underlie other, more common forms of vasculitis and stroke whose causes are currently unknown.

Genetic Changes

ADA2 deficiency is caused by mutations in the *CECR1* gene. This gene provides instructions for making an enzyme called adenosine deaminase 2. Studies suggest that this enzyme plays an essential role in keeping the lining of blood vessel walls intact. It also appears to be involved in the growth and development of certain immune system cells, including macrophages, which are a type of white blood cell that plays a critical role in inflammation. Some macrophages are pro-inflammatory, meaning they promote inflammation, while others are anti-inflammatory, meaning they reduce inflammation.

Mutations in the *CECR1* gene severely reduce or eliminate the function of adenosine deaminase 2. Researchers do not fully understand how a loss of this enzyme's function leads to the features of ADA2 deficiency. They speculate that a lack of this enzyme may

disrupt the balance between pro-inflammatory and anti-inflammatory macrophages in various tissues, leading to abnormal inflammation. The enzyme's role in maintaining the structural integrity of blood vessels could help explain why the blood vessels are most often affected by inflammation in this disorder.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- ADA2 deficiency
- childhood-onset polyarteritis nodosa
- DADA2
- deficiency of ADA2
- Sneddon syndrome

Diagnosis & Management

These resources address the diagnosis or management of adenosine deaminase 2 deficiency:

- Genetic Testing Registry: Polyarteritis nodosa
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0031036/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Polyarteritis Nodosa
  https://medlineplus.gov/ency/article/001438.htm
- Health Topic: Ischemic Stroke
  https://medlineplus.gov/ischemicstroke.html
- Health Topic: Vasculitis
  https://medlineplus.gov/vasculitis.html

Genetic and Rare Diseases Information Center

- Adenosine Deaminase 2 deficiency
  https://rarediseases.info.nih.gov/diseases/12383/adenosine-deaminase-2-deficiency
- Polyarteritis nodosa
  https://rarediseases.info.nih.gov/diseases/7360/polyarteritis-nodosa
- Sneddon syndrome
  https://rarediseases.info.nih.gov/diseases/7664/sneddon-syndrome

Additional NIH Resources

- National Heart, Lung, and Blood Institute: What is Vasculitis?
  https://www.nhlbi.nih.gov/health/health-topics/topics/vas
- National Institute of Neurological Disorders and Stroke: Stroke Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Stroke-Information-Page

Educational Resources

- Disease InfoSearch: Sneddon syndrome
  http://www.diseaseinfosearch.org/Sneddon+syndrome/6652
- MalaCards: sneddon syndrome
  http://www.malacards.org/card/sneddon_syndrome
- NIH News: NIH team discovers genetic disorder causing strokes and vascular inflammation in children (February 19, 2014)
  https://www.genome.gov/27556385/
- Orphanet: Sneddon syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=820

- Orphanet: Vasculitis due to ADA2 deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=404553
- The Merck Manual Home Edition: Overview of Vasculitis
  http://www.merckmanuals.com/home/bone-joint-and-muscle-disorders/vasculitic-disorders/overview-of-vasculitis

Patient Support and Advocacy Resources

- American Stroke Association
  http://www.strokeassociation.org/STROKEORG/AboutStroke/StrokeInChildren/Stroke-In-Children_UCM_308543_SubHomePage.jsp
- National Organization for Rare Disorders (NORD): Polyarteritis Nodosa
  https://rarediseases.org/rare-diseases/polyarteritis-nodosa/
- National Stroke Association
  http://www.stroke.org/understand-stroke/impact-stroke/pediatric-stroke
- Vasculitis Foundation
  http://www.vasculitisfoundation.org/
- YoungStroke
  http://youngstroke.org/

Genetic Testing Registry

- Polyarteritis nodosa
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0031036/

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28adenosine+deaminase+2+deficiency%5BTIAB%5D%29+OR+%28DADA2%5BTIAB%5D%29+OR+%28ADA2+deficiency%5BTIAB%5D%29%29+OR+%28%28childhood%5BTIAB%5D%29+AND+%28polyarteritis+nodosa%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- POLYARTERITIS NODOSA, CHILDHOOD-ONSET
  http://omim.org/entry/615688
- SNEDDON SYNDROME
  http://omim.org/entry/182410

Sources for This Summary

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